

Exhibit A

Clean Version of The Pending Claims in U.S. Patent Application Ser. No. 09/691,343

4. (Original) An isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence first disclosed in the NHP gene described in SEQ ID NO:6.

5. (Previously Presented) An isolated nucleic acid molecule comprising a nucleotide sequence that:

- (a) encodes the amino acid sequence shown in SEQ ID NO:7; and
- (b) hybridizes to the nucleotide sequence of SEQ ID NO:6 or the complement thereof under highly stringent conditions of 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

6. (Original) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO:7.

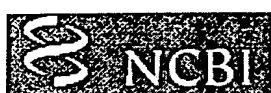
7. (Previously Presented) A recombinant expression vector comprising the isolated nucleic acid molecule of claim 4.

8. (Previously Presented) A host cell comprising the recombinant expression vector of claim 7.

9. (Previously Presented) The isolated nucleic acid molecule of claim 4, comprising the nucleic acid sequence of SEQ ID NO:6.

10. (Previously Presented) The recombinant expression vector of claim 7, wherein said nucleic acid molecule encodes the amino acid sequence shown in SEQ ID NO:7.

11. (Previously Presented) The recombinant expression vector of claim 10, wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO:6.

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PubMed	Nucleotide	Protein	Genome	Structure	PMC	Taxonomy	OMIM	Bc
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1: Nat Cell Biol 2000 May;2(5):302-9 Related Articles, Link

cell biology

PDGF-C is a new protease-activated ligand for the PDGF alpha-receptor.

Li X, Ponten A, Aase K, Karlsson L, Abramsson A, Uutela M, Backstrom G, Hellstrom M, Bostrom H, Li H, Soriano P, Betsholtz C, Hedin CH, Alitalo K, Ostman A, Eriksson U.

Ludwig Institute for Cancer Research, Stockholm, Sweden.

Platelet-derived growth factors (PDGFs) are important in many types of mesenchymal cell. Here we identify a new PDGF, PDGF-C, which binds to and activates the PDGF alpha-receptor. PDGF-C is activated by proteolysis and induces proliferation of fibroblasts when overexpressed in transgenic mice. *In situ* hybridization analysis in the murine embryonic kidney shows preferential expression of PDGF-C messenger RNA in the metanephric mesenchyme during epithelial conversion. Analysis of kidneys lacking the PDGF alpha-receptor shows selective loss of mesenchymal cells adjacent to sites of expression of PDGF-C mRNA; this is not found in kidneys from animals lacking PDGF-A or both PDGF-A and PDGF-B, indicating that PDGF-C may have a unique function.

PMID: 10806482 [PubMed - indexed for MEDLINE]

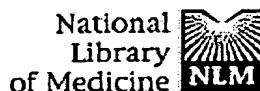
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1: *J Biol Chem* 2001 Jul 20;276(29):27406-14

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Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor.

Gilbertson DG, Duff ME, West JW, Kelly JD, Sheppard PO, Hofstrand PD, Gao Z, Shoemaker K, Bukowski TR, Moore M, Feldhaus AL, Humes JM, Palmer TE, Hart CE.

ZymoGenetics Inc., Seattle, Washington 98102, USA. gilbertd@zgi.com

We have characterized platelet-derived growth factor (PDGF) C, a novel growth factor belonging to the PDGF family. PDGF-C is a multidomain protein with the N-terminal region homologous to the extracellular CUB domain of neuropilin-1, and the C-terminal region consists of a growth factor domain (GFD) with homology to vascular endothelial growth factor (25%) and PDGF A-chain (23%). A serum-sensitive cleavage site between the two domains allows release of the GFD from the CUB domain. Competition binding and immunoprecipitation studies on cells bearing both PDGF alpha and beta receptors reveal a high affinity binding of recombinant GFD (PDGF-CC) to PDGF receptor-alpha homodimers and PDGF receptor-alpha/beta heterodimers. PDGF-CC exhibits greater mitogenic potency than PDGF-AA and comparable or greater mitogenic activity than PDGF-AB and PDGF-BB on several mesenchymal cell types. Analysis of PDGF-CC in vivo in a diabetic mouse model of delayed wound healing showed that PDGF-CC significantly enhanced repair of a full-thickness skin excision. Together, these studies describe a third member of the PDGF family (PDGF-C) as a potent mitogen for cells of mesenchymal origin in *in vitro* and *in vivo* systems with a binding pattern similar to PDGF-AB.

PMID: 11297552 [PubMed - indexed for MEDLINE]

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Frame = +3

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Links

LOCUS PDGFC 3007 bp mRNA linear PRI 17-AUG-2001

DEFINITION *Homo sapiens* platelet derived growth factor C (PDGFC), mRNA.

ACCESSION NM_016205

VERSION NM_016205.1 GI:9994186

KEYWORDS

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ORGANISM *Homo sapiens*
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REFERENCE 1 (bases 1 to 3007)

AUTHORS Li,X., Ponten,A., Aase,K., Karlsson,L., Abramsson,A., Uutela,M., Backstrom,G., Hellstrom,M., Bostrom,H., Li,H., Soriano,P., Betsholtz,C., Heldin,C.H., Alitalo,K., Ostman,A. and Eriksson,U.

TITLE PDGF-C is a new protease-activated ligand for the PDGF alpha-receptor

JOURNAL Nat. Cell Biol. 2 (5), 302-309 (2000)

MEDLINE 20268201

PUBMED 10806482

REFERENCE 2 (bases 1 to 3007)

AUTHORS Hamada,T., Ui-Tei,K. and Miyata,Y.

TITLE A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/VEGF family

JOURNAL FEBS Lett. 475 (2), 97-102 (2000)

MEDLINE 20317014

PUBMED 10858496

REFERENCE 3 (bases 1 to 3007)

AUTHORS Tsai,Y.J., Lee,R.K., Lin,S.P. and Chen,Y.H.

TITLE Identification of a novel platelet-derived growth factor-like gene, fallotein, in the human reproductive tract

JOURNAL Biochim. Biophys. Acta 1492 (1), 196-202 (2000)

MEDLINE 20461776

PUBMED 11004490

REFERENCE 4 (bases 1 to 3007)

AUTHORS Zwerner,J.P. and May,W.A.

TITLE PDGF-C is an EWS/FLI induced transforming growth factor in Ewing family tumors

JOURNAL Oncogene 20 (5), 626-633 (2001)

MEDLINE 21214457

PUBMED 11313995

REFERENCE 5 (bases 1 to 3007)

AUTHORS Uutela,M., Lauren,J., Bergsten,E., Li,X., Horelli-Kuitunen,N., Eriksson,U. and Alitalo,K.

TITLE Chromosomal location, exon structure, and vascular expression patterns of the human PDGFC and PDGFC genes

JOURNAL Circulation 103 (18), 2242-2247 (2001)

MEDLINE 21266739

PUBMED 11342471

REFERENCE 6 (bases 1 to 3007)
AUTHORS Gilbertson, D.G., Duff, M.E., West, J.W., Kelly, J.D., Sheppard, P.O., Hofstrand, P.D., Gao, Z., Shoemaker, K., Bukowski, T.R., Moore, M., Feldhaus, A.L., Humes, J.M., Palmer, T.E. and Hart, C.E.
TITLE Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor
JOURNAL J. Biol. Chem. 276 (29), 27406-27414 (2001)
MEDLINE 21347863
PUBMED 11297552
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Revised: July 5, 2002.

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NCBI Nucleotide

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

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Links

LOCUS AF260738 1804 bp mRNA linear PRI 17-JUL-2001

DEFINITION *Homo sapiens* platelet-derived growth factor C (PDGFC) mRNA, complete cds.

ACCESSION AF260738

VERSION AF260738.1 GI:14009503

KEYWORDS

SOURCE *Homo sapiens* (human)

ORGANISM *Homo sapiens*
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 1804)

AUTHORS Gilbertson, D.G., Duff, M.E., West, J.W., Kelly, J.D., Sheppard, P.O., Hofstrand, P.D., Gao, Z., Shoemaker, K., Bukowski, T.R., Moore, M., Feldhaus, A.L., Humes, J.M., Palmer, T.E. and Hart, C.E.

TITLE Platelet-derived growth factor C (PDGF-C), a novel growth factor that binds to PDGF alpha and beta receptor

JOURNAL J. Biol. Chem. 276 (29), 27406-27414 (2001)

MEDLINE 21347863

PUBMED 11297552

REFERENCE 2 (bases 1 to 1804)

AUTHORS Gao, Z., Hart, C., Piddington, C., Sheppard, P., Shoemaker, K., Gilbertson, D., West, J. and O'Hara, P.J.

TITLE Direct Submission

JOURNAL Submitted (26-APR-2000) Biomolecular Informatics, ZymoGenetics, Inc., 1201 Eastlake Avenue East, Seattle, WA 98102, USA

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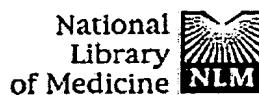
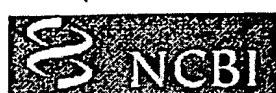
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Revised: July 5, 2002.

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1: Biochim Biophys Acta 2000 Jun 21;1492(1):196-202

Related Articles, Link

ELSEVIER SCIENCE
FULL-TEXT ARTICLE

Identification of a novel platelet-derived growth factor-like gene, fallottein, in the human reproductive tract.

Tsai YJ, Lee RK, Lin SP, Chen YH.

Division of Reproduction and Endocrinology, Department of Medical Research, Mackay Memorial Hospital, Tamshui, Taiwan.
yjtsai@ms1.mmh.org.tw

We isolated the cDNA of a novel platelet-derived growth factor-like gene from human endometrium. The gene was named fallottein; it was 3007 bases in length, and encoded a protein of 345 amino acids. Antiserum against the fallottein protein can recognize a specific protein in the fallopian tube, with a molecular size in accordance with the anticipated size of fallottein. Fallottein mRNA is expressed in two molecular sizes, 3.8 and 2.9 kb, with the former being more abundant. High expression of the gene was found in the prostate, testis, and uterus. A weaker expression signal was found in the spleen, thymus, and small intestine, but expression of fallottein in the colon and peripheral blood leukocytes was negligible.

PMID: 11004490 [PubMed - indexed for MEDLINE]

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Mar 3 2003 10:01:4

>AF091434 ACCESSION:AF091434 NID: gi 6002592 gb AF091434.1 AF091434
Homo sapiens secretory growth factor-like protein
fallotein mRNA, complete cds
Length = 3007

Score = 486 bits (1237), Expect = e-135
Identities = 234/234 (100%), Positives = 234/234 (100%)
Frame = +3

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1: AF091434. Homo sapiens secr...[gi:6002592]

LOCUS AF091434 3007 bp mRNA linear PRI 22-JUN-2000

DEFINITION Homo sapiens secretory growth factor-like protein fallotain mRNA, complete cds.

ACCESSION AF091434

VERSION AF091434.1 GI:6002592

KEYWORDS

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 3007)

AUTHORS Tsai, Y.J., Lee, R.K., Lin, S.P. and Chen, Y.H.

TITLE Identification of a novel platelet-derived growth factor-like gene, fallotain, in the human reproductive tract

JOURNAL Biochim. Biophys. Acta 1492 (1), 196-202 (2000)

MEDLINE 20461776

PUBMED 11004490

REFERENCE 2 (bases 1 to 3007)

AUTHORS Tsai, Y.J., Lee, R.K.K. and Lin, S.P.

TITLE Direct Submission

JOURNAL Submitted (14-SEP-1998) Dept. Medical Research, Mackay Memorial Hospital, 45 Min Sheng Road, Tamshui, Taipei County 25115, Taiwan

FEATURES Location/Qualifiers

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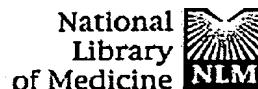
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Revised: July 5, 2002.



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1: FEBS Lett 2000 Jun 16;475(2):97-102

Related Articles, Link

EISEVIER SCIENCE
FULL-TEXT ARTICLE

A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/VEGF family.

Hamada T, Ui-Tei K, Miyata Y.

Department of Pharmacology, Nippon Medical School, Tokyo, Japan.

We isolated a novel gene designated spinal cord-derived growth factor (SCDGF). Its expression was increased in chick spinal cords with embryonic development and decreased after hatching. The amino acid sequences of chick and human SCDGFs revealed a putative signal sequence followed by a CUB domain and a region homologous to the members of the platelet-derived growth factor/vascular endothelial growth factor family. Furthermore, human SCDGF secreted from the cells showed a mitogenic activity for 10T1/2 cells in vitro. These results led us to speculate that SCDGF plays an important role in the development of the spinal cord.

PMID: 10858496 [PubMed - indexed for MEDLINE]

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Mar 3 2003 10:01:4

>AB033831 ACCESSION:AB033831 NID: gi 9392293 dbj AB033831.1 Homo sapiens hSCDGF mRNA for spinal cord-derived growth factor, complete cds Length = 1817

Score = 486 bits (1237), Expect = e-135
Identities = 234/234 (100%), Positives = 234/234 (100%)
Frame = +3

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1: AB033831. Homo sapiens hSCD...[gi:9392293]

Links

LOCUS AB033831 1817 bp mRNA linear PRI 26-JUL-2000

DEFINITION Homo sapiens hSCDGF mRNA for spinal cord-derived growth factor, complete cds.

ACCESSION AB033831

VERSION AB033831.1 GI:9392293

KEYWORDS spinal cord-derived growth factor; scdgf gene.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (sites)

AUTHORS Hamada,T., Ui-Tei,K. and Miyata,Y.

TITLE A novel gene derived from developing spinal cords, SCDGF, is a unique member of the PDGF/VEGF family

JOURNAL FEBS Lett. 475 (2), 97-102 (2000)

MEDLINE 20317014

PUBMED 10858496

REFERENCE 2 (bases 1 to 1817)

AUTHORS Hamada,T., Ui-Tei,K. and Miyata,Y.

TITLE Direct Submission

JOURNAL Submitted (25-OCT-1999) Tsuyoshi Hamada, Nippon Medical School, Department of Pharmacology; 1-1-5, Sendagi, Bunkyo-ku, Tokyo 113-8602, Japan (E-mail:t-hamada@nms.ac.jp, Tel:81-3-3822-2131(ex.5277), Fax:81-3-5814-1684)

FEATURES

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1321 atgaggagtg tgactgtgtg tgcagagggc gcacaggagg atagccgat caccaccaggc
1381 agctcttgc caaagctgtg cagtgcagt gctgattcta taaaagaacg tatgcgttat
1441 ctccatcctt aatctcagtt gtttgcattca aggaccttcc atcttcagga ttacagtgc
1501 attctgaaag aggagacatc aaacagaatt aggagttgtg caacagctct ttgagagga
1561 ggcctaaagg acaggagaaa aggtttcaa tcgtggaaag aaaaattaaat gttgtattaa
1621 atagatcacc agctagtttcc agagttacca ttttgcattca tccactagct gggttctgt
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1741 agtgatcacc tgattccgtt gccttgcctt actctaaagc tccatgtcct gggcctaaaa
1801 tcgtataaaaa tctggat

//

Revised: July 5, 2002.

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Mar 3 2003 10:13:39

**Query= SEQ ID NO:6
(918 letters)**

Sequences producing significant alignments: Score E
(bits) Value

AC092608.2.1.196952 430 e-118
AC093325.3.1.130754 236 2e-59

>AC092608.2.1.196952
Length = 196952

>AC092608.2.1.196952

Score = 430 bits (217), Expect = e-118
Identities = 217/217 (100%)
Strand = Plus / Minus

Query: 702 agtagataattatgaaaaggaaaaatctgaagaccaactttacaaatattggcaga 761
Sbjct: 74905 agtagataattatgaaaaggaaaaatctgaagaccaactttacaaatattggcaga 74846

Score = 414 bits (209), Expect = e-113
Identities = 209/209 (100%)
Strand = Plus / Minus

Query: 496 caattcacagaagctgtgagtccttcagtgctaccccttcagcttgcactggacctg 555
Sbjct: 77153 caattcacagaagctgtgagtccttcagtgctaccccttcagcttgcactggacctg 77094

Query: 556 cttataatgtataactgccttagtaccttggaaagaccttattcgatatcttgaacca 615
Sbjct: 77093 cttataatgtataactgccttagtaccttggaaagaccttattcgatatcttgaacca 77034

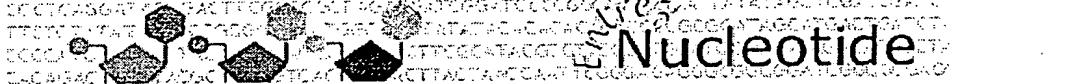
Query: 616 gagagatggcagttggacttagaagatctatataaggccaaacttggcaacttcttggcaag 675
Sbjct: 77033 gagagatggcagttggacttagaagatctatataaggccaaacttggcaacttcttggcaag 76974

>AC093325.3.1.130754
Length = 130754

Score = 236 bits (119), Expect = 2e-59
Identities = 119/119 (100%)
Strand = Plus / Minus

Query: 1 atgagcctttcgggcttctcctgctgacatctgcctggccggccagagacagggact 60
||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct: 80211 atgagcctttcgggcttctcctgctgacatctgcctggccggccagagacagggact 80152

Query: 61 caggcggaatccaacctgagtagtaaattccagtttccagcaacaaggAACG 119
||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Sbjct: 80151 caggcggaatccaacctgagtagtaaattccagtttccagcaacaaggAACG 80093

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1: AC092608. Homo sapiens BAC ...[gi:15668121]

Links

LOCUS AC092608 196952 bp DNA linear PRI 01-MAR-2002

DEFINITION Homo sapiens BAC clone RP11-154F14 from 4, complete sequence.

ACCESSION AC092608 AC009582

VERSION AC092608.2 GI:15668121

KEYWORDS HTG.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 196952)

AUTHORS Sulston,J.E. and Waterston,R.

TITLE Toward a complete human genome sequence

JOURNAL Genome Res. 8 (11), 1097-1108 (1998)

MEDLINE 99063792

PUBMED 9847074

REFERENCE 2 (bases 1 to 196952)

AUTHORS Isak,A., Kozlowicz,A. and Hawkins,M.

TITLE The sequence of Homo sapiens BAC clone RP11-154F14

JOURNAL Unpublished (2001)

REFERENCE 3 (bases 1 to 196952)

AUTHORS Waterston,R.H.

TITLE Direct Submission

JOURNAL Submitted (19-JUL-2001) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 4 (bases 1 to 196952)

AUTHORS Waterston,R.H.

TITLE Direct Submission

JOURNAL Submitted (19-SEP-2001) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 5 (bases 1 to 196952)

AUTHORS Waterston,R.

TITLE Direct Submission

JOURNAL Submitted (01-MAR-2002) Department of Genetics, Washington University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA

COMMENT On Sep 19, 2001 this sequence version replaced gi:14916193.

----- Genome Center
Center: Washington University Genome Sequencing Center
Center code: WUGSC
Web site: <http://genome.wustl.edu/gsc>
Contact: sapiens@watson.wustl.edu

----- Summary Statistics
Center project name: H_NH0154F14
Drafting Center: WIBR

NCBI

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Links

1: AC093325. Homo sapiens BAC ...[gi:15982602]

LOCUS AC093325 130754 bp DNA linear PRI 09-JAN-2002

DEFINITION Homo sapiens BAC clone RP11-612J15 from 4, complete sequence.

ACCESSION AC093325

VERSION AC093325.3 GI:15982602

KEYWORDS HTG.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

REFERENCE 1 (bases 1 to 130754)
AUTHORS Sulston, J.E. and Waterston, R.

TITLE Toward a complete human genome sequence

JOURNAL Genome Res. 8 (11), 1097-1108 (1998)

MEDLINE 99063792

PUBMED 9847074

REFERENCE 2 (bases 1 to 130754)
AUTHORS Waligorski, J. and Haakenson, W.

TITLE The sequence of Homo sapiens BAC clone RP11-612J15

JOURNAL Unpublished (2002)

REFERENCE 3 (bases 1 to 130754)
AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (18-AUG-2001) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 4 (bases 1 to 130754)
AUTHORS Waterston, R.H.

TITLE Direct Submission

JOURNAL Submitted (07-OCT-2001) Genome Sequencing Center, Washington University School of Medicine, 4444 Forest Park Parkway, St. Louis, MO 63108, USA

REFERENCE 5 (bases 1 to 130754)
AUTHORS Waterston, R.

TITLE Direct Submission

JOURNAL Submitted (09-JAN-2002) Department of Genetics, Washington University, 4444 Forest Park Avenue, St. Louis, Missouri 63108, USA

COMMENT On Oct 7, 2001 this sequence version replaced gi:15624997.

----- Genome Center
Center: Washington University Genome Sequencing Center
Center code: WUGSC
Web site: <http://genome.wustl.edu/gsc>
Contact: sapiens@watson.wustl.edu

----- Summary Statistics
Center project name: H_NH0612J15

NOTICE: This sequence may not represent the entire insert of this